
DIFFUSION AND CARRIER
TRANSPORT OF IONS IN CHARGED
MEMBRANES

*A comparative study of transport processes
and electrical phenomena in solid and liquid ion
exchange membranes*

By

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Upps. Uppsala.



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DIFFUSION AND CARRIER TRANSPORT OF IONS IN CHARGED MEMBRANES

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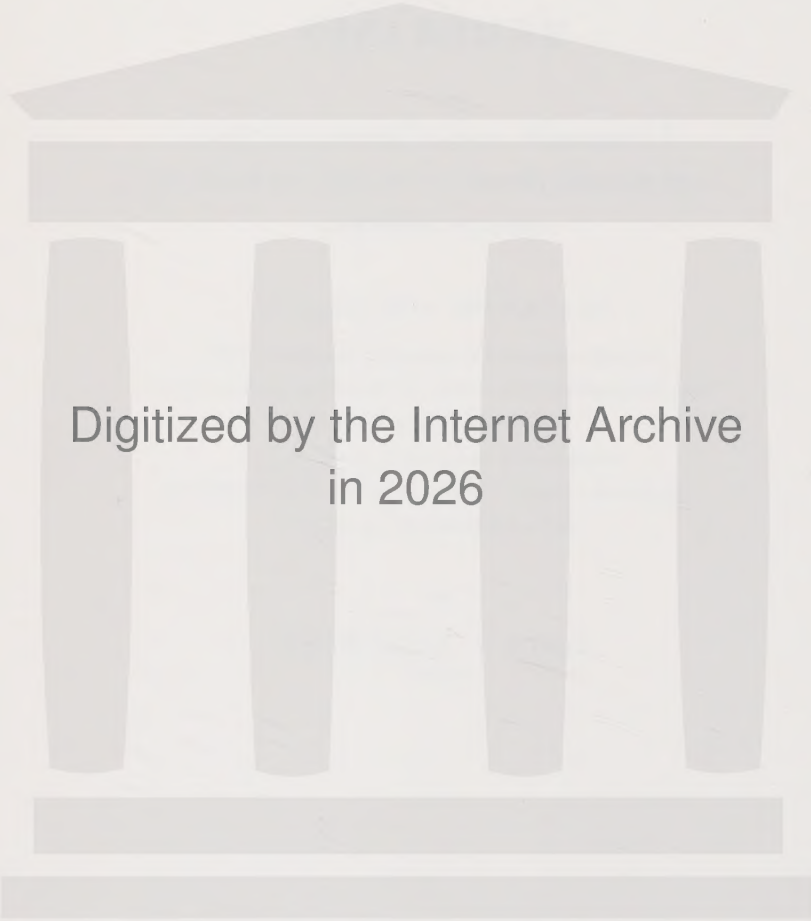
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This thesis is a summary of the following papers referred to in the text by their roman numerals.

- I. J. SANDBLOM, A method to relate steady-state ionic currents conductances, and membrane potential in ion exchange membranes with unknown thermodynamic properties. *Biophys. Journ.* 7, 243 (1967).
- II. J. SANDBLOM, G. EISENMAN, and J. L. WALKER, Jr., Electrical phenomena associated with the transport of ions and ion pairs in liquid ion exchange membranes. I. Zero current properties. *J. Phys. Chem.* In press (1967).
- III. J. SANDBLOM, Transport processes and ion pair formation in liquid membranes. *Arkiv för Fysik.* In press (1967).
- IV. J. SANDBLOM, G. EISENMAN and J. L. WALKER, Jr., Electrical phenomena associated with the transport of ions and ion pairs in liquid ion exchange membranes. II. Non-zero current properties. *J. Phys. Chem.* In press (1967).
- V. J. SANDBLOM, Liquid ion exchange membranes with weakly ionized groups. I. A theoretical study of their steady-state properties.
- VI. J. SANDBLOM, Liquid ion exchange membranes with weakly ionized groups. II. The resistance and EMF of a thin membrane.

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Introduction

The nature of ion permeation in living membranes is one of the main problems of biophysics and several different methods have been used in attempts to reach a solution [1]. One important approach which has revealed the physical nature of many bioelectrical phenomena and other properties of cell membranes has been to correlate the structure and transport processes in artificial membranes [2, 3]. Since the behavior of a membrane is governed by two factors, namely the structure of the membrane and the driving forces on the permeating species, the use of model systems in which these factors can be varied in a controlled manner have provided important clues and criteria for determining the structure of cell membranes as well as the possible types of mechanisms of ion migration [4].

Although the detailed molecular structure of a cell membrane is still unknown, experimental evidence [5, 6] seems to indicate that it behaves like a charged barrier to the transfer of ions, where the charges may either be rigidly anchored to the membrane phase [7], free to move within the membrane boundaries in the form of lipid soluble carriers [8] or located at the surface in the form of particular macromolecular structures acting as "gates" [9]. Since these charges will act as binding sites for the ions in solution a cell membrane may be classified as an ion exchange membrane, i.e. a membrane containing dissociable groups confined to the membrane phase. These groups, constituting the sites for exchange, may either be fixed or mobile, organic or inorganic, associated or dissociated as seen from Fig. 1 which shows a classification of ion exchange membranes according to their structure and chemical composition [4].

A wide variety of porous membranes (i.e. groups (1) and (2) of Fig. 1) have been studied as models for biological membranes particularly with respect to their electric and osmotic behavior [12-14]. Recently, however, a great deal of interest has also been devoted to membranes with very pronounced ion selective properties belonging to groups (3), (4) and (6) of Fig. 1. Their high degree of ionic selectivity, allowing them to be used as ion specific electrodes [15, 16], is also a property which makes them very attractive as models for biological membranes [4]. The present investigation is therefore devoted to transport phenomena in these highly selective ion exchange membranes which have previously only been subject to treatments in very specialized cases [17-19]. Before summarizing the results, however, a brief description of ion exchange membranes will be given with particular reference to the types included in this investigation.

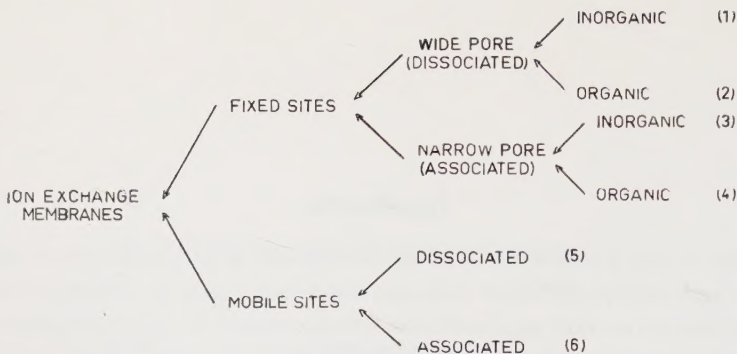


Fig. 1. A classification of ion exchange membranes according to their structure and chemical composition. (1) Loosely compacted minerals and sectioned minerals; (2) loosely crosslinked resins and "wet" collodion; (3) glass electrodes and highly compacted minerals; (4) tightly cross-linked resins, dried collodion and oil-impregnated millipore filters; (5) strongly acidic or basic liquid exchangers; (6) weakly acidic or basic liquid exchangers (in low dielectric constant liquids). A detailed description of these various types of membranes may be found in textbooks [10] or review articles [11] on ion exchange membranes.

The structure of ion exchange membranes

The total behavior of an ion exchange membrane may be seen as a combination of transport processes in the membrane phase and of ion exchange processes at the boundaries. From this point of view it is useful to consider the membrane phase and membrane boundaries as separate structures.

I. Membrane phase

1. Solid ion exchange (fixed site) membranes

The most important parameters that determine the behavior of fixed site membranes are the site density and the pore size. In membranes with very wide pores the specific interactions between the ions in the pores and the fixed sites lining the pore walls may be neglected and the sites and counter ions may therefore be regarded as completely dissociated [4]. The transport processes are then exclusively determined by diffusion of ions in the aqueous channels and by convective movement of water through the pores, as a consequence of which the mobilities may be considered as constants. At the boundaries the ions will partition according to Donnan equilibria.

A completely different set of properties is characteristic of membranes with very small pores. In this case the pores are so small that aqueous channels no longer exist and the diffusion of ions takes place by a site to site migration. As a result of this type of ion migration mechanism the possibility exists for the ionic mobilities to be strongly concentration dependent [20, 21]. In the absence of channels the sites and

counter ions will also be closely spaced and in view of their strong mutual electrostatic interaction they may be regarded as strongly associated. The ion exchange properties in this case will no longer be described by simple Donnan equilibria determined by the site density. Instead the field surrounding the sites will tend to exclude the co-ions from the membrane phase and its strength will determine the sequence and magnitude of selectivity for the counter ions. This is the basic principle for using certain materials, e.g. glass, as ion specific electrodes.

Eisenman [22] has made a systematic study of the specificity of glass electrodes and has shown that a similar set of sequences is characteristic both of biological membranes and glass membranes suggesting that the local field strength of the sites may play an important role in the transfer of ions in biological membranes.

2. Liquid ion exchange (mobile site) membranes

The dissociable groups of liquid ion exchange membranes are free to move within the membrane boundaries but are more or less confined to the membrane phase, often referred to as the oil phase. Despite the fact that no pores or channels exist in these membranes the important distinction between dissociated and associated sites may still be made in mobile site membranes analogous to the situation in fixed site membranes. Dissociated sites are produced by such acidic or basic exchangers as dinitronaphthalene sulphonic acid and quaternary ammonium salts whereas strongly associated sites are obtained with weakly acidic or basic exchangers, e.g. alkyl phosphoric acids or alkyl amines [23].

Association between sites and counter ion in a liquid membrane implies that a permeable component will be transported partly in the form of free ions and partly in combination with the sites in the form of electroneutral ion pairs. Since this phenomenon may be considered as a kind of carrier transport of ions, liquid ion exchange membranes may be regarded as models for the lipid soluble carriers postulated to exist in biological membranes [8, 24].

The strong association between sites and counter ions will also give rise to differences in affinity of the membrane for the various ions, a property which has been used in developing liquid ion exchange membrane into electrodes sensitive particularly to divalent cations [16].

II. Membrane boundaries

The properties of ion exchange membranes are not only determined by their internal structure but also by the nature of the boundaries. An ideal boundary between two thermodynamic phases is geometrically a surface of discontinuity and should not exhibit any resistance to the transfer of ions. However, the external solutions will always contain unstirred layers next to the membrane phase and the effects of these are determined by the rate of diffusion in the membrane and by its thick-

ness [10]. Since, however, the present treatment is only concerned with transport phenomena inside the membrane, the thickness of the membrane is assumed to be large enough for any film effects to be neglected.

In liquid membranes there is also the possibility for the two phases to become structured at the area of contact. Such particular surface structures are known to have very high activation energies [25, 26] and will therefore act as barriers to the entry of ions. On the other hand if an ion exchanger is dissolved in the oil phase it will presumably be oriented at the surface in such a way that the polar groups will extend into the aqueous phases and facilitate the formation of ion pairs between sites and counter ions. Such a process will tend to decrease the surface resistance.

As long as interfacial processes do not constitute the rate limiting step, as will be assumed in the following, the membrane phase may be considered to be in thermodynamic equilibrium with the external solutions at the interfaces. The exchange of ions across the boundary may therefore be described by a set of equilibrium conditions although an important distinction must be made between solid and liquid ion exchange membranes. Whereas the ion exchange equilibria of fixed site membranes are determined purely by the distribution of ions between membrane and solution, the sites of the liquid membrane will always dissolve to a certain extent in the aqueous solutions and thereby contribute to the boundary reactions. The extent to which this effects the membrane properties has been discussed by Bonhoeffer *et al.* [17]. It is possible, however, to choose a liquid ion exchanger with a high preference for the membrane phase which permits the solubility of the sites in the external solutions to be neglected in certain concentration ranges [27], and the boundary conditions can then be written in the same way as for a fixed site membrane as demonstrated in paper II and applied in the subsequent treatments (papers III–VI).

The physical properties of ion exchange membranes

The structural differences and similarities between solid and liquid ion exchange membranes will be reflected in their physical properties. In general these are most easily related to the membrane structure under conditions of steady-state and which has been successfully and extensively done in the case of porous (dissociated) fixed site membranes [12–14] and mobile (dissociated) site membranes [19]. *The purpose of the present investigation is therefore to characterize the steady state properties of strongly associated solid and liquid ion exchange membranes partly as an attempt to distinguish between diffusion and carrier transport of ions in biological membranes and partly to examine the parameters governing electrode specificity in ion exchange membranes.* Considerations are restricted to homogeneous membranes. For fixed site membranes the flux equations have been solved taking into account the effects of concentration dependent mobilities (*Paper I*) and the results have also been applied to experimental observations on a thin hydrated glass membrane. In *papers*

II and *III* a general theory for liquid ion exchange membranes in which ion pair formation takes place has been developed and the complete solutions to the equations for two special cases are given in *papers IV* and *V*, namely the case of a single counter ion (*paper IV*) and the case of weakly dissociated sites (*paper V*). The results of *paper IV* have been verified experimentally on a model system [28] and the results of *paper V* have been tested on a thin liquid ion exchange membrane (*paper VI*).

I. *Fixed (associated) site membranes*

Teorell [12], Meyer and Sievers [29] followed by others [13, 14] have studied the properties of porous fixed site membranes under steady state conditions and have developed theories relating transport phenomena to such parameters as fixed site density, hydrodynamic permeability and applied forces (e.g. electrical, osmotic and pressure forces). These theories have been based on the assumptions of constant mobilities in the membrane and Donnan equilibria at the boundaries.

A corresponding description of non-porous fixed site membranes must also take into account the effects of ion site interactions which will influence both the chemical properties and the ionic mobilities. A steady state solution to the equations describing the transport of ions in these membranes was first given by Conti and Eisenman [18] who considered a case in which the mobilities were functions only of the site properties (i.e. field strength and site density). However, Eisenman and Sandblom [20] have studied a thin hydrated glass membrane as a model for biological membranes and their experimental observations indicated that the mobilities are not only dependent on the site properties but also strongly dependent on the local concentrations in this membrane. Possibly this may be due to a vacancy mechanism of migration. To take this phenomena into account, however, a different method for solving the flux equations in the steady state must be used and is presented in paper I. Instead of the usual procedure of separating boundary and interior processes [18], the concept of corresponding solutions is used to determine the local ionic conductances. Treating the membrane like a "black box" it is shown how these can be calculated at any point in the membrane from two sets of measurements, (a) R_{symm} , the steady state resistance of the membrane measured between identical solutions and (b) V_0 , the potential difference between non-identical solutions for zero currents. These two parameters are measured for several external solution compositions (e.g. a varying sodium potassium ratio ranging from zero to infinity). Using the calculated ionic conductances the flux equations are integrated without a knowledge of mobilities, activity coefficients and other interior membrane parameters. This method has been applied to glass membranes and proved to be very useful for predicting the electric behavior and transport properties of these membranes [20].

It turns out that several of the equations derived by this general method are

similar or identical to the equations derived for porous membranes using the Teorell-Meyer Sievers theory [2] and for biological membranes using the constant field assumption [30]. However, whereas these theories always permit a calculation of concentration profiles and potential profiles within the membrane, the present method, due to the non-specific assumptions, leaves the profiles undetermined. It is therefore concluded quite generally in paper I that *characterization of transport phenomena alone, such as fluxes and potentials for various solution conditions is not sufficient to specify the internal concentrations and potential profiles for an unknown membrane*. This requires a completely different category of measurements equivalent to measuring the equilibrium properties of the membranes, e.g. ion exchange isotherms. Detailed information about the site properties of a non-porous, fixed site membrane can therefore only be obtained by measuring both fluxes and ion exchange isotherms.

II. Mobile (associated) site membrane

Liquid membranes as models for biological membranes were first described by Beutner [3] who measured the potentials of concentration cells made from various oils. By studying the effects of adding oleophilic salts he was able to show that the phase boundaries responded as electrodes to changes in external solution conditions, which he suggested to be the origin of the membrane potential. Another important step was taken by Bonhoeffer *et al.* [17] who used the concepts of the Teorell-Meyer-Sievers theory to predict the e.m.f. of liquid ion exchange membranes taking into account also the internal transport processes.

One of the main differences between fixed and mobile site membranes concerns the rearrangeability of the sites in the latter. This was recognized by earlier workers [17] but studied in more detail by Conti and Eisenman [19] who treated the case of complete dissociation between sites and counter ions. An applied electric field was shown to produce a redistribution of the sites in the membrane with a depletion at one end of the membrane and a corresponding accumulation at the other end. This concentration polarization was shown to be directly related to the applied potential and, in an ideally permselective membrane, the sites were shown to become completely depleted at one end of the membrane at a certain limiting current, causing the resistance to become infinite [19]. Mobile site membranes are therefore characterized by the existence of finite limiting currents as opposed to fixed site membranes whose conductances approach limiting values as the applied fields is increased.

Additional features distinguishing fixed and mobile site membranes appear through the formation of ion pairs or other higher order aggregates in the latter. This effect has been introduced in a more general treatment of homogeneous, ideally permselective liquid ion exchange membranes, described in papers II and III. Two special cases of this general treatment are considered in more detail in papers IV and V, namely the single counter ion case and the case of weakly dissociated sites with several counter ions.

1. General case

In paper II the flux equations for a multicomponent system of univalent electrolytes are derived by considering the free ions and the ion pairs as separately flowing entities. Dissociated and associated species, called subcomponents, are assumed to be in chemical equilibrium at every point in the membrane and their concentrations are related to each other by the law of mass action. The boundary conditions are obtained by assuming the sites to be completely trapped in the membrane phase while the counter ions are free to exchange across the boundaries. From this set of equations the total behavior of the system may be established, and has partly been accomplished in papers III–V.

A number of general properties deduced from these equations are presented in paper III. In this paper the equations of paper II are used to derive a set of phenomenological equations relating the total fluxes of the permeable components to the corresponding driving forces. The derivation also yields a set of relationships between the phenomenological coefficients and the parameters of the subcomponents (i.e. their mobilities and concentrations) and from these relationships some important conclusions about the membrane properties are obtained:

(1) The phenomenological cross coefficients have a *negative* sign implying that *the flow of a species in one direction induces a coupled flow of another species in the opposite direction*. This phenomenon is called *counter transport* in the biological literature and is generally used as a criterion for carrier transport [8].

(2) From the diagonal elements of the coefficient matrix another property characteristic of carrier transport is deduced, namely *facilitated diffusion*. This implies that *the flux of a tracer utilizes the carriers to give a larger permeability than that measured from membrane resistance* [24]. The same conclusion is also derived in paper IV in an slightly different way.

(3) The transport of ions in two different forms will impart certain properties of heterogeneity to the membrane, which are summarized in the equivalent circuit for a membrane element. From this circuit it is apparent that *not only the free ions but also the electroneutral ion pairs contribute to the electric current*, which is merely a consequence of recirculation of the sites within the membrane, as may be deduced from the equations.

The equivalent circuit is shown to have two branches each with different properties permitting a formal distinction between the diffusion pathway of ion pairs and the diffusion pathway of free ions, although geometrically the membrane constitutes a homogeneous thermodynamic phase. This aspect of heterogeneity, characteristic of a homogeneous liquid ion exchange membrane, is relevant to the behavior of biological membranes through which ions have been proposed to move in different channels [31, 32].

It is worth while to emphasize that the treatments of fixed and mobile site mem-

branes presented in papers I and III are equally general and do not contain any assumptions about mobilities and activity coefficients in the membrane. The results may therefore be seen as a thermodynamic proof that *the three properties outlined above are sufficient criteria for distinguishing diffusion and carrier transport in membranes whose detailed structure is unknown*, e.g. biological membranes.

2. Special cases

Additional information about the properties of liquid ion exchange membranes are obtained by making more specific assumptions about the parameters, such as constant ionic mobilities and activity coefficients and which has been done in the two cases presented in papers IV and V.

(a) *Single counter ion*

This particular case is treated in paper IV where the general flux equations derived in paper II are integrated under the specific assumptions mentioned.

It is shown that the parameters necessary to characterize the membrane in this case are the dissociation constant (K), the limiting conductance (λ_0), the transference numbers (t) of sites and counter ions and finally the mobility (u_{1s}) of the ion pairs. All of these parameters can be determined by classical electrochemical methods except for the mobility of the ion pairs, which may be calculated from the value of the limiting current by using an expression derived in paper IV.

From the explicit solutions to the flux equation given in paper IV it is also shown that the current-voltage relationship becomes increasingly linear with increasing association, an effect which is due to the "buffering" action of the ion pairs. These will not be acted on by electric forces and will therefore oppose the redistribution of sites under an applied electric field, resulting in a more ohmic response. It is also shown that increasing association causes an increased discrepancy between the ionic permeability obtained from measurements of tracer diffusion and that obtained from measurements of the electric resistance, which is a result of facilitated diffusion as previously mentioned.

Paper IV concludes with a discussion of the physical systems to which the analysis is applicable, particularly the conditions required for the sites to behave as trapped. A model system in which this condition is satisfied has been devised by Walker *et al.* [28] for the purpose of testing the theory. It consists of a polyvinyl tubing containing a solution of HCl in isopropyl alcohol and sealed at both ends with AgCl electrodes. In this model the membrane is that part of the system which is enclosed between the AgCl-electrodes and it contains all the ingredients of a liquid ion exchange membrane, namely a permeable counterion (Cl⁻ions), a trapped site (H⁺-ions) and ion pairs (HCl molecules). The basic parameters, K , λ_0 , t_H and t_{Cl} for this system were determined by classical electrochemical methods and u_{HCl} was obtained from the value

of the limiting current. Inserting these values in the theoretical equations of paper IV a good agreement between theoretically predicted and experimentally observed profiles and current voltage relationships was obtained [28].

(b) *Weakly dissociated sites*

Paper V is devoted to a special case of practical importance, namely that of weakly dissociated groups characteristic of most conventional liquid ion exchange membranes [33]. It is also the case which most closely resembles the type of carrier models described in the biological literature [8] in which the diffusion of free ions in the membrane phase is implicitly neglected.

The membrane properties for this particular case are deduced by assuming that the number of free ions is very small compared to the number of ion pairs. By introducing a number of additional, idealizing assumptions the flux equations are integrated for a multicomponent system of univalent electrolytes, and the profiles, fluxes and membrane resistance are expressed in terms of the electric current. It is shown that the current voltage relationship is practically linear for intermediate fields whereas higher fields give rise to a nonlinearity which depends not only on the mobilities of the counter ions but also on their dissociation constants.

The shape is therefore distinctly different from that of fixed site membranes which exhibit a rectification for intermediate fields depending upon the magnitude of the ionic permeabilities (paper I). For comparison the current voltage characteristics for the two types of membranes are shown in fig. 2. The circles represent experimentally measured values and the dotted curves are calculated theoretically. A slightly better agreement between theory and experiment is seen to be obtained with a solid membrane (fig. 2a) than with a liquid membrane (fig. 2b) the reason being that fewer parameters and assumptions are needed in order to characterize the behavior of solid membranes.

One of the most important measurements used to characterize ion exchange membranes is V_0 , the membrane potential at zero current. The significance of this potential, referred to as "resting potential" in biological membranes and "electrode potential" in the case of electrodes, lies in the fact that it permits a direct evaluation of the ionic permeabilities. For liquid ion exchange membranes with weakly dissociated sites an expression for V_0 in the case of two univalent counter ions is derived in paper II. It is given by:

$$V_0 = \frac{RT}{ZF} (1 - \tau) \ln \frac{a'_1 + \frac{k_2}{k_1} \cdot \frac{\lambda_{02}}{\lambda_{01}} \cdot a'_2}{a''_1 + \frac{k_2}{k_1} \cdot \frac{\lambda_{02}}{\lambda_{01}} \cdot a''_2} + \frac{RT}{ZF} \cdot \tau \ln \frac{a'_1 + \frac{k_2}{k_1} \cdot \frac{K_1}{K_2} \cdot \frac{u_{2s}}{u_{1s}} \cdot a'_2}{a''_1 + \frac{k_2}{k_1} \cdot \frac{K_1}{K_2} \cdot \frac{u_{2s}}{u_{1s}} \cdot a''_2}$$

where

$$\tau = \frac{\lambda_{0s}(K_1 u_{2s} - K_2 u_{1s})}{\lambda_{01} K_1 u_{2s} - \lambda_{02} K_2 u_{1s}}$$

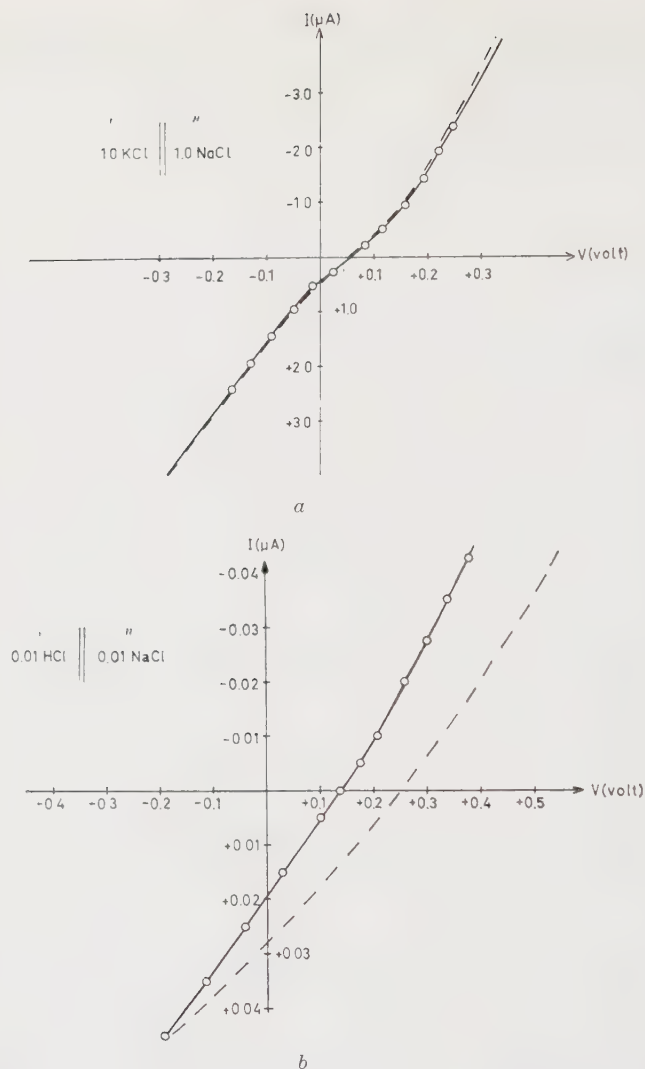


Fig. 2. Current voltage characteristics for a) a glass membrane and b) an oil membrane interposed between solutions having the indicated compositions. Positive current flows from left to right in the indicated systems and the solution on the left side is considered to have ground potential. The circles represent experimentally measured values and the dotted curves are calculated theoretically from the equations of paper I and V, using the measured parameters.

The superscripts refer to the two sides of the membrane and the subscripts to the counter ions and sites. a_1, a_2 are the activities in the external solutions and k_2/k_1 is the limiting partition coefficient of the counter ions at infinite dilution in the membrane phase. R, T and F have their usual meaning.

The expression for V_0 is seen to be composed of two logarithmic terms correspond-

ing to the two mentioned pathways, namely that of the free ions and that of the ion pairs. The first term therefore contains the properties of the membrane phase expressed by the limiting partition coefficients and conductances, whereas the second term also contains the site properties expressed by the dissociation constants and the mobilities of the ion pairs.

For fixed site membranes V_0 reduces to the first term (paper I) which is also recognized as the constant field equation used to describe the resting potential of cell membranes [30]. *Fixed site membranes are therefore characterized by a single set of ionic permeabilities, while mobile (associated) site membranes, due to their electrical heterogeneity, are characterized by two sets of ionic permeabilities as seen from the equation given above.*

It is also shown in paper II that this electrode equation which reveals the factors responsible for the ionic specificity of liquid ion exchange membranes is not only valid in the steady state but in the transient state as well, even when no precautions are taken to avoid convective mixing in the interior of the membrane. *This also proves the important fact that the potential response, following step changes in the external solution conditions, is instantaneous.* The same conclusion has previously been made for fixed site membranes [34, 35].

(c) *The simultaneous presence of completely dissociated and strongly associated counter-ions*

A membrane containing both completely dissociated and strongly associated counterions is treated as a special case in paper V and such a system is shown to possess "apparent" limiting conductances for intermediate fields and limiting currents for fields approaching infinity. *Therefore the conductance limited I-V-curves characteristic of biological membranes do not exclude the possibility for the presence of ionic carriers, which could conceivably be detected by the appearance of limiting currents if sufficiently high fields were applied.*

III. *Experimental observations on a thin membrane*

Previous experiments designed to study the properties of oil membranes have generally been carried out on thick non-convection free systems, which have not permitted the attainment of a steady-state [17, 33, 36]. A method has therefore been developed by which an oil drop is placed in a small hole drilled in a thin lucite disc and where it forms a stable membrane in contact with the aqueous solutions. This method is described in paper VI and has the advantage over previously described experimental arrangements in that it permits a study of the steady-state membrane properties.

The membrane is formed by dissolving the acid cation exchanger di-2-ethyl-hexyl phosphoric acid in amyl alcohol and is shown to conform reasonably well with the assumptions on which the theories are based, notably completely trapped sites and a

convection free membrane. With this system the steady-state theories developed in the previous papers can be tested in particularly the conclusions of paper V, and it is also suitable for comparing liquid and solid ion exchange membranes with respect to rectification and other steady-state properties, a comparison which the previously studied non-convection free liquid membranes have not permitted.

In this system simultaneous measurements have been made of the transient membrane resistance and e.m.f. following step changes in external solution conditions. From the results it is concluded that the e.m.f. is established instantaneously long before the profiles have reached their steady states. Measurements of the steady state membrane resistance are also described in paper VI, and confirm the theoretical predictions that the resistance is practically independent of the electric field but strongly dependent on the external solution compositions.

Experiments have also been performed in concentration ranges where the coions have not been excluded and under those conditions the membrane shows a strong rectification tendency, which is not predicted by the theory. It is suggested that this phenomenon is due to interactions between Cl-ions and water molecules leading to changes in the water content of the membrane.

Concluding remarks

The results presented in papers I–VI have demonstrated several features that may be used in distinguishing diffusion and carrier transport of ions in biological membranes. These may shortly be discussed in relation to observations made on biological membranes where several active processes involving secretion, absorption and the maintenance of uneven ionic distributions across cell membranes appear to be strong evidence for the existence of carrier transport. On the other hand such observed phenomena as limiting conductances, the strong rectification tendency and the absence of carrier currents seem rather to favor the involvement of diffusion processes.

In paper III it was shown that liquid ion exchange membranes exhibit many characteristic features common to biological membranes, particularly the phenomenon of counter transport, which also contains the possibility for uphill movement, i.e. movement against the electrochemical gradient. This raises the question whether liquid ion exchange membranes could be used as models for active transport, defined as the uphill movement of a species at the expenditure of metabolic energy. Such a model was studied by Osterhout [37] using guajacol as a membrane and by adjusting the pH on the two sides he was able to demonstrate an uphill movement of a cation such as potassium across the membrane. However, in this model as well as in the homogeneous ion exchange membranes studied here, the only forces acting on the system are external, and, according to strict thermodynamic definitions these systems

are not capable of primary active transport [38, 39]. Nevertheless the phenomenon of counter transport is a typical example of *secondary* active transport, a term used by Hoshiko and Lindley [39] to indicate that a component is transported against its electrochemical gradient without being directly entrained by a metabolic reaction.

Another phenomenon, characteristic of carrier transport, is the discrepancy between flux and electric measurements which has also been observed in biological membranes, e.g. for the bromide transport across the gall bladder [40]. Such a discrepancy is expected in liquid but not in solid ion exchange membranes.

Concerning the electrical properties of the membrane it was shown in paper V that in the presence of weakly ionized groups, when most of the ionic transport occurs in the form of ion pairs, the membrane resistance is practically linear. Since a cell membrane such as the squid axon is known to have a high rectification tendency, *the transport processes in these membranes can therefore not be due exclusively to carriers but also to a certain extent to diffusion processes*. On the other hand it was also pointed out in paper V that *the limiting conductances characteristic of the squid axon membrane is not conclusive evidence for pure a diffusion process* since mobile site membranes may in some cases exhibit apparent limiting conductances.

The heterogeneous character of biological membranes where the ions are proposed to move in separate channels is also in some aspects characteristic of liquid ion exchange membranes which was shown in paper III. The diffusion of ions and ion pairs will create two partly connected electrical pathways and a particular component will have a definite affinity for each of these pathways. This is analogous to the situation in the squid axon which is proposed to have one sodium-carrying system with a particular set of specificities for the alkali cations and another potassium-carrying system with a different set of specificities for these ions [32]. It should be emphasized, however, that the systems studied in this investigation have been homogeneous and with the subcomponents assumed to be in chemical equilibrium at every point in the membrane. Therefore the equivalent circuit for the *whole* membrane cannot be described by two completely separated branches each with a time variant resistance as in the case of the squid axon membrane [41].

In applying the conclusions obtained from studies on artificial membranes to biological membranes it is important to consider the approximations involved. Although the theoretical assumptions such as thermodynamic equilibrium at the boundaries and microscopic electroneutrality at all points in the system are valid for the macroscopic systems described, these may not at all be valid for biological membranes in which even the standard equations of irreversible thermodynamics may not be applicable. These and other points concerning the validity of macroscopic treatments in biological membranes have been discussed by Agin [42]. It must therefore be concluded that whereas the equations and theories presented may be directly applicable to such laboratory systems as electrodes their applicability to phenomena encountered in living systems may entirely be qualitative.

General summary

The steady state properties of non-porous solid and liquid ion exchange membranes used as models for biological membranes have been subject to theoretical and experimental analysis in attempts to characterize their electric properties and to distinguish between diffusion and carrier transport of ions. The following results have been obtained.

(1) The equations governing the steady state properties of nonporous solid ion exchange membranes have been derived, taking into account a possible concentration dependence of the chemical properties and the mobilities. These equations have subsequently been applied to thin hydrated glass membranes from which it has been concluded that their behavior is completely predictable from two sets of measurements, the membrane potential at zero current and the resistance measured between identical solutions.

(2) A corresponding set of equations have also been derived for liquid ion exchange membranes in which sites and counter ions have been assumed to form electro-neutral ion pairs. This has enabled the properties associated with carrier transport of ions to be deduced, as well as the factors governing electrode specificity in liquid ion exchange membranes.

(3) To test the theoretical predictions of transport phenomena in liquid ion exchange membranes a method has been developed allowing the membrane properties to be studied under steady-state conditions. A thin, stable, convention free membrane has been obtained by placing the ion exchanger (di-2-ethyl-hexyl phosphoric acid in amyl alcohol) in a small hole drilled through a lucite disc. On this system the electric properties of liquid ion exchange membranes have been examined and compared with the theoretically predicted behavior.

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